REMARKS

In the Official Action dated June 20, 2007, Claims 31-41, 44 and 45 are pending. The Examiner states that the Applicants' elected species (NiTPP-VLFFA) is free of the prior art. Claim 34 is objected to for certain misspelling of a term. Claims 31-40 and 45 are rejected under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter. Claims 31-41, 44 and 45 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Claims 31-41, 44 and 45 are also rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. Claims 31-37, 40, 41, 44 and 45 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by WO 96/40148 A1 to Malfroy-Camine. Claims 31-41, 44 and 45 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over WO 96/40148 in view of U.S. Patent No. 5,004,697 to Pardridge.

This Response addresses each of the Examiner's objections and rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Before addressing the merits of the Official Action, Applicants direct the Examiner's attention to the amendment to the claims. Claims 31-36 and 38-46 have been canceled without prejudice, and Claims 47-55 are added. Support for Claims 47-55 is found in the specification, e.g., at page 4, lines 20-24, page 5, line 24, page 8, line 8 and lines 19-20, page 11, lines 1-6, page 10, lines 9-11; page 15, lines 20-23; and page 22, lines 10-13. No new matter is introduced by the addition of Claims 47-55. Applicants reserve the right to file a continuation application to pursue the subject matter of Claims 31-36 and 38-46 as previously filed.

Claim 34 is objected to for misspelling the term "loop." Applicants submit that the objection is moot in view of the cancellation of Claim 34. Applicants further submit that the new claims correctly recite the term "loop." Withdrawal of the objection is respectfully requested.

Claims 31-40 and 45 are rejected under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter. The Examiner alleges that Claims 31-40 and 45, as previously presented, can be interpreted as a naturally biological process, e.g., circulating hemoglobin, ceruloplasmin, and insulin contacting amyloid protein in the brain.

Applicants respectfully submit that the rejection is moot in view of the cancellation of Claims 31-40 and 45. Applicants further submit that Claims 47-55 clearly recite a method of solubilizing Aβ deposited in the brain of an Alzheimer's disease patient by administering certain metal complex to the patients. Thus, Claims 47-55 are not directed to a naturally occurring process that is unpatentable under 35 U.S.C. §101. Applicants therefore request withdrawal of the rejection under 35 U.S.C. §101.

Claims 31-41, 44 and 45 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner alleges that Claims 31-41, 44 and 45 are directed to inhibiting the binding of metal ions to the β-amyloid peptide or treating Alzheimer's disease with a metal complex. The Examiner contends that the claims, as written, encompass any metal complex. The Examiner acknowledges that methods of making metal complexes are known to the one skilled in the art. However, the Examiner alleges that methods of making the myriad of compounds that will be capable of functioning as required in the claims is beyond the knowledge of a skilled artisan. The Examiner admits that the specification provides sufficient written description with respect to metal complex BRI7161, BRI7159, BRI7158, BRI7080 or BRI7103 and compounds specifically identified in the specification tables and/or examples. However, the Examiner states that the possible structural variations of a metal complex are limitless. The Examiner alleges that the specification lacks sufficient description for a variety of species to reflect this variance in the genus. The Examiner

is of the opinion that one would not know which compound to make in order to practice the method as claimed beyond BRI7161, BRI7159, BRI7158, BRI7080 or BRI7103.

In the first instance, Applicants respectfully submit that the rejection is moot in view of the cancellation of Claims 31-41, 44 and 45. Applicants further submit that Claims 47-55 now clearly define the metal complex, i.e., the metal is selected from the group consisting of Mn, Co, Ni, Cu, Zn, Ru, Pd, Ag, Cd, Pt, Au, Rh and Hg. Moreover, Applicants respectfully submit that the specification on page 4, lines 20-24, teaches that the compound binds to at least one histidine residue selected from the group consisting of His6, His13 and His14 of the N-terminal loop of β-amyloid peptide. Applicants submit that the specification on page 8, lines 19-25 and page 11, lines 1-21 further delineates that metal ions capable of binding to the imidoazole nitrogen of histindine include Mn, Co, Ni, Cu, Zn, Ru, Pd, Ag, Cd, Pt, Au, Rh and Hg, and complexes of these metals are expected to react with beta-amyloid. The specification on page 14, line 1 to page 15, line 23, and page 22, Table 1 and lines 10-16, describes specific examples of metal complexes for use in conjunction with the methods claimed by the present application.

Accordingly, Applicants respectfully submit that the specification provides sufficient written description in such a way to convey one skilled in the art that the present inventors had possession of the invention, as presently claimed, at the time the present application was filed. Therefore, in view of the foregoing, Applicants respectfully request withdrawal of the written description rejection under 35 U.S.C. §112, first paragraph.

Claims 31-41, 44 and 45 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. The Examiner acknowledges that the specification enables inhibiting the binding of metal ions to β-amyloid peptide with BRI7161, BRI7159, BRI7158, BRI7080 or BRI7103 or the compounds specifically identified in the specification and prior art.

However, the Examiner alleges that the specification does not provide enablement for inhibition of the binding of metal ions to the β-amyloid peptide, or treating Alzheimer's disease with all or any metal complexes. According to the Examiner, the specification has provided compounds asserted to be useful in the methods and provides *in vitro* testing and *ex vivo* (e.g. NMR) testing for several compounds. However, the Examiner alleges that the specification does not provide sufficient guidance, including working or prophetic examples, to show that any compound, other than BRI7161, BRI7159, BRI7158, BRI7080 or BRI7103, would work in treating Alzheimer's disease.

In the first instance, Applicants respectfully submit that the present invention is predicated in part on the elucidation that a metal complex, which prevents binding of metal ions to the beta-amyloid protein by competing with the metal ions for at least one histidine residue of Aβ, can thereby solubilize aggregated beta-amyloid deposits in the brains of individuals with Alzheimer's disease. Applicants respectfully submit that prior to the present invention it had been believed that treatment of Alzheimer's disease required binding of the free metal ions, which would therefore not be available for binding to the Aβ. Thus, Applicants respectfully submit that the present invention provides a unique approach to the treatment of Alzheimer's disease.

Moreover, Claims 31-41, 44 and 45 are canceled, and Claims 47-55 now define the metal complex to be a Mn, Co, Ni, Cu, Zn, Ru, Pd, Ag, Cd, Pt, Au, Rh or Hg complex. As discussed above with respect to the written description rejection, the specification on page 4, lines 20-24, teaches that the compound binds to at least one histidine residue selected from the group consisting of His6, His13 and His14 of the N-terminal loop of β-amyloid peptide. Applicants submit that the specification on page 8, lines 19-25 and page 11, lines 1-21 further

delineates that metal ions capable of binding to the imidoazole nitrogen of histindine include Mn, Co, Ni, Cu, Zn, Ru, Pd, Ag, Cd, Pt, Au, Rh and Hg, and complexes of these metals are expected to react with beta-amyloid. The specification on page 14, line 1 to page 15, line 23, and page 22, Table 1 and lines 10-16 describes specific examples of metal complexes for use in conjunction with the methods claimed by the present application.

Accordingly, Applicants respectfully submit that the specification provides sufficient guidance for one skilled in the art to make recited metal complex and use them in the presently claimed method, without undue experimentation. Therefore, in view of the foregoing, Applicants respectfully request withdrawal of the enablement rejection under 35 U.S.C. §112, first paragraph.

Claims 31-37, 40, 41, 44 and 45 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by WO 96/40148 A1 to Malfroy-Camine. The Examiner alleges that Malfroy-Camine teaches a method for preventing, arresting or treating a free radical-associated disease, including Alzheimer's, by the administration of certain salen metal complex.

Applicants observe that the salen metal complex disclosed by Malfroy-Camine is characterized by a general formula as shown in the reference, as well as on page 10 of the Official Action. Applicants respectfully submit that the salen metal complex described by Malfroy-Camine is not able to block Aβ deposited in the brain of an Alzheimer's disease patient.

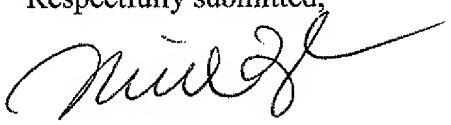
Accordingly, Applicants respectfully submit that the presently presented claims recite metal complexes that are distinguished from that described by Malfroy-Camine. Therefore, in view of the foregoing, Applicants respectfully submit that the rejection is moot and Claims 46-55 are not anticipated by Malfroy-Camine. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102(b) with respect to Malfroy-Camine.

Claims 31-41, 44 and 45 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Malfroy-Camine in view of U.S. Patent No. 5,004,697 to Pardridge. The Examiner is of the opinion that the primary reference to Malfroy-Camine teaches treating Alzheimer's with a metal salen complex, but does not teach coupling the metal salen complex with a targeting moiety. The Examiner alleges that Pardridge teaches modifying antibodies for delivery through the BBB for neuropharmaceuticals and the antibody in Pardridge is for amyloid peptide of Alzheimer's disease. The Examiner alleges that it would have been obvious to have made and delivered the metal salen complex via coupling to an amyloid specific antibody in order to specifically deliver the salen complex to the Alzheimer's plaques that the metal salen complex is used to treat.

Applicants respectfully submit that Claims 31-41, 44 and 45 have been canceled and the presently presented claims recites metal complexes that are distinguished from that described in Malfroy-Camine. The secondary reference to Pardridge does not ameliorate the deficiencies of the primary reference to Malfroy-Camine. Therefore, in view of the cancellation of the Claims 31-41, 44 and 45 and addition of Claims 46-55, Applicants respectfully submit that the obviousness rejection is moot and Claims 46-55 are not obvious in view of Malfroy-Camine and Pardridge. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103(a) with respect to Malfroy-Camine and Pardridge.

In view of foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



Xiaochun Zhu
Registration No. 56,311

Scully, Scott, Murphy & Presser, P.C.
400 Garden City Plaza, Suite 300
Garden City, New York 11530
(516) 742-4343
ZY:ab